REMARKS

Claims 1, 2, 9, 10, 12-15 and 17-38 are currently pending in the application. With this Response, claims 1, 9, 10, 13, 14 and 15 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added. With these amendments, Applicant respectfully requests reconsideration and allowance of claims 1, 2, 9, 10 and 12-15.

With the current Response, Applicant has amended independent claim 1 to limit the claim to tissue samples; as such, independent claim 1 excludes an array comprising DNA or RNA samples which have been extracted from various tissue samples (as is the subject of the Lincoln et al. reference and the Lehman et al. reference). All dependent claims have been similarly amended. Further, independent claim 1 has been amended to replace the term "for placement of" with the term "having"; as such, the Applicant has sought to clarify the structural limitations of independent claim 1. As amended, Applicant believes the claims of the pending application are not anticipated by the Lincoln et al. reference or made obvious by the Lincoln et al. reference in view of the Schraml et al. reference and/or the Lehman et al. reference. Therefore, Applicant respectfully requests reconsideration and allowance of claims 1, 2, 9, 10 and 12-15.

Claims Rejected Under 35 U.S.C. §102:

The Office Action rejected claims 1, 2, 10, 12-13, and 15 under 35 U.S.C. §102(e)(2) as being anticipated by U.S. Patent No. 6,553,317 to Lincoln et al. With this Response, Applicant has amended independent claim 1 in order to overcome the above-identified rejection. More specifically, the Applicant has amended independent claim 1 to limit the claim to a microarray having only tissue samples--as such, a nucleic acid array is outside the scope of the claims as amended. In addition, the applicant has amended independent claim 1 to remove the phrase "for placement of" in order to clarify the intended structural limitations of the claim. Applicant believes that the above-identified amendments overcome the anticipation rejection to Lincoln et al. Therefore, Applicant respectfully requests reconsideration and allowance of claims 1, 2, 10, 12-13 and 15.

The Lincoln et al. reference discloses a relational database system for storing biomolecular sequence information together with biological annotations detailing the source of the sequence information, and associated reagent information. More specifically, the Lincoln et al. reference discloses:

> The present invention provides relational database systems for **storing biomolecular sequence information together with biological annotations detailing the source of the sequence information, and associated reagent information.** The acquisition, storage and access of reagent information associated with databased biomolecular sequence information is a particular advantage of the present invention. **Such reagent information identifies genetic information and materials which may be made available to a user of the relational database system of the present invention for further application in research, therapeutic pharmaceutical development or other fields.** The reagent information aspect of the present invention is preferably used in conjunction with a biomolecular sequence relational database system. (the Lincoln et al. reference; Col. 2, Lines 14-28)(Emphasis added).

The above-identified passage indicates the primary disclosure of the Lincoln et al. reference. DNA or RNA is sequenced and the sequence information is stored in a database. The sequence information may then be compared against various publicly available sequence information in order to identify various relationships. The Lincoln et al. reference continues:

> **The present invention further provides a reagent clone identified by a process, at least partially implemented on a computer system, for establishing a set of reagent clones. The process involves grouping initial sequences of polynucleotide inserts in a plurality of clones into a master cluster, assembling the initial sequences of the master cluster into one or more contiguous sequences, such that relationships of sequences to each other in the master cluster are elucidated, and nominating at least one clone represented by a master cluster as a reagent clone, according to specified priority criteria.** A set of reagent clones may also be nominated according to such a method. **The set of reagent clones may have a variety of uses including as hybridizable elements on a biological microarray**. (the Lincoln et al. reference; Col. 2, Line 66-Col 3, Line12)(Emphasis added).

In the above-identified passage, a utility of the present invention is identified. The present invention allows for a set of reagent clones to be identified. Once identified, the reference indicates that the reagent clones may be used as a hybridizable element on a prior art biological

microarray. Such a disclosure does not appear to anticipate a tissue microarray of the present invention; the above-disclosure merely indicates that microarrays exist and the Lincoln et al. references discloses a method of determining hybridizable elements that may be used in conjunction with these prior art microarrays.

Next, the Lincoln et al reference discloses how the database is populated:

> Referring initially to FIG. 1A, a process that may be employed to initially populate relational databases in accordance with this invention is shown. The process begins at a step 6 in which **clones from a particular tissue or cell type are sequenced**. Specifically, scientists extract mRNA from a sample under consideration (e.g., a particular tissue or cell line) and construct fully complex cDNA libraries. Thereafter, automated sequencing equipment sequences 3000 to 5000 clone templates, for example, from the resulting cDNA library.
>
> The sequences obtained from step 6 provide the initial population of the relational database. **The present invention also provides for the selection and further sequencing of certain clones to form a reagent set**. This process is described below. (the Lincoln et al. reference; Col. 4, Lines 41-55)(Emphasis added).

As such, a clone is extracted from a tissue or a cell. Next, the clone is sequenced. Following sequencing, the sequence information is inputted into a database. As such, a tissue microarray is never constructed.

The Office Action cited the following passage of the Lincoln et al. reference to indicate the presence of a tissue microarray:

> **In a preferred embodiment, clones undergoing resequencing for verification are processed in groups ("lots") of 96 clones, one for each chamber of a 96-well plastic culture dish (each chamber/well is an indentation in the dish that can hold a liquid such as a bacterial culture separate from all the others).** After verification, clones that "pass" are re-racked (transferred) into new lots for storage. When reagent clones and associated data are provided to third parties, such as customers purchasing the clones for further research, the reagent clones are preferably shipped in these lots. A customer receiving clones and their sequences must know not only that the clone has been received, but also its precise location, if s/he is to make use of the reagent. Lot and Well information is recorded for each reagent clone that passes the post-

> nomination processing to tell the customer where to find the clone. (EG clone 1234567 is located in lot #14332, well #G03). (the Lincoln et al. reference; Col. 12, Lines 20-36)(Emphasis added).

The above-identified passage indicates that a 96-well plate may be used to sequence the same clone 96 times as a method of verifying the sequence of the clone. More specifically, the sequence of a clone is verified by sequencing the same clone 96 times and comparing the 96 results. As such, the microarray of the above identified passage does not appear to anticipate the oncology tissue microarray of the present invention.

The Office Action identified passages from the Lincoln et al. reference which discloses a Tissue Database (see Col. 16, Lines 7-43 of the Lincoln et al. reference.) These passages disclose that the Lincoln et al. database includes information about the tissue from each clone that was selected. However, the passages do not disclose the use of any type of tissue microarray.

In summary, the Lincoln et al. reference discloses a system wherein various clones are extracted from various tissue samples. The clones are then sequenced and the sequence information is inputted into a database. The sequence information may then be compared to publicly available sequence information and various relationships may be determined. However, the Lincoln et al. reference does not disclose any type of microarray. The reference merely states that: (1) the clones identified by the database of the invention may be used with prior art microarrays; and (2) the sequence of a clone may be verified by sequencing the same clone 96 times in a 96-well plate. Although the Lincoln et al. reference does not appear to disclose any type of microarray, for the purpose of expediting prosecution, Applicant has amended independent claim 1 to comprise only tissue samples--i.e., not nucleic acid samples.

As amended, Applicant believes the current claims are not anticipated by the Lincoln et al. reference because the Lincoln et al. reference does not disclose a tissue microarray of the present invention. More specifically, the Lincoln et al. reference does not disclose a profile array substrate comprising **a first location having a test tissue, a second location having a control oncology tissue microarray** comprising **a plurality of tissue samples**, each tissue sample stably associated with a distinct, known sublocation on a substrate, at least one tissue sample

comprising a normal tissue sample, the control oncology tissue microarray comprising tissue samples representing the progression of cancer from an early stage to an advanced stage, the substrate further comprising an identifier providing access to a database comprising information relating to each patient from whom each tissue sample of the control oncology tissue microarray was obtained, wherein the profile array substrate allows testing of the test tissue to be done simultaneously with the testing of the tissue samples on the control oncology tissue microarray allowing for a side-by-side comparison of the test tissue with the tissue samples in the control oncology tissue microarray.

With these amendments to the claims of the present invention, Applicant respectfully requests reconsideration and allowance of claims 1, 2, 10, 12-13, and 15.

Claims Rejected Under 35 U.S.C. §103:

The Office Action rejected claims 1-2, 9-10, and 12-15 under 35 U.S.C. §103(a) as being unpatentable over the Lincoln et al. patent in view of the Schraml et al. reference (Clinical Cancer Research, August 1999, vol. 5, pages 1966-1975) and the Lehman et al. reference (Cancer Research, February 2000, vol. 60, pages 1062-1069).

As discussed above, the Lincoln et al. reference does not anticipate the amended claims of the present invention. Further, Applicant does not believe that either the Schraml et al. reference or the Lehman et al. reference, individually or in any combination, cure the deficiencies of the Lincoln et al. reference.

Like the Lincoln et al. reference, the Lehman et al. reference discloses extracting DNA or RNA from a biological sample (blood), sequencing the DNA and inputting the sequence information into a database. More specifically, the Lehman et al. reference discloses:

> ...A protocol for the study was approved by the Human Investigations Committee at Yale University School of Medicine, and all patients signed a written informed consent form. Samples were coded and entered into a double-blinded database. The enrolled familial breast cancer patients underwent an extensive interview for complete family history with a three-generation pedigree profile. **After the interview, all enrolled patients underwent sterile phlebotomy, from which 10-15 ml of blood was**

> **collected for genomic DNA isolation from lymphocytes.** (Lehman et al., pgs. 1062-1063)(Emphasis added).

As such, the Lehman et al. experiments did not use tissue microarrays; the Lehman et al. experiments were conducted by arraying genomic DNA obtained from blood samples.

Next, in discussing the use of microarray technology, the Lehman et al. reference discloses:

> ...Therefore, we investigated the frequency of both exon and intron germ-line p53 base changes in 42 breast cancer patients with a strong family history of breast cancer. **Purified DNA obtained from the 42 indexed cases was screened for germ-line p53 mutations in exons 2-11 and surrounding introns using a combination of intron based primers for PCR-SSCP analysis, direct sequencing, and microarray sequencing using the Affymetrix p53 gene chip methodology**...(Lehman et al., p. 1063)(Emphasis added).

As such, like Lincoln et al., Lehman et al. merely discloses using microarray technology to efficiently sequence 42 samples to determine which of these 42 samples comprises a genetic mutation of interest. Therefore, the Lehman et al. reference does not cure any of the deficiencies of the Lincoln et al. reference.

Next, the Schraml et al. reference discloses the use of a tissue microarray to identify three known oncogenes in a plurality of different types of cancerous tissue. The Schraml et al. reference discloses:

> Gene amplifications are common in many different tumor types and may confer diagnostic, prognostic, or therapeutic information for patient management. Tedious experiments are often required to determine which tumor types have amplifications of a specific oncogene. **To facilitate rapid screening for molecular alterations in many different malignancies, a tissue microarray consisting of samples from 17 different tumor types was generated. Altogether, 397 individual tumors were arrayed in a single paraffin block.** To determine whether results from the literature can be reproduced on minute tissue samples (diameter, 0.6mm), amplification of three extensively studied oncogenes (CCND1, CMYC, and ERBB2) was analyzed in three fluorescence in situ hybridization experiments from consecutive sections cut from the tissue microarray...(Schraml et al., Abstract)(Emphasis added).

As such, the Schraml et al. reference merely discloses the use of a tissue microarray to rapidly analyze a plurality of samples for a certain characteristic. The Applicant is not claiming to have invented the concept of using a tissue microarray. However, as amended, the Applicant claims a device which utilizes the benefits of microarray technology (speed, efficiency) to compare a test tissue sample with a plurality of known tissue samples. Furthermore, a database is incorporated into the system in order to determine relationships between the various tissue samples and the test specimen. Such a system provides a powerful diagnostic tool in various fields of medicine. Such a system is not disclosed, taught or suggested in the Schraml et al. reference.

With this Response, the Applicant has made an earnest effort to respond to all issues raised in the Office Action of January 14, 2005, and to place all claims in condition for allowance. As amended, the current claims recite a profile array substrate comprising a first location having a test tissue and a second location having a oncology tissue microarray. Further, the oncology microarray comprises only tissue sample--i.e., not nucleic acid samples. The cited art does not disclose, teach or suggest such a profile array substrate. As such, the Applicant respectfully requests reconsideration and allowance of pending claims 1-2, 9, 10 and 12-15.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

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Name: Michael P. Doyle
Registration No.: 49,052
Customer No.: 29932
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel. (617) 239-0100